Enzymatic preparation of optically active carboxylic acid derivatives using ochrobactrum anthropi

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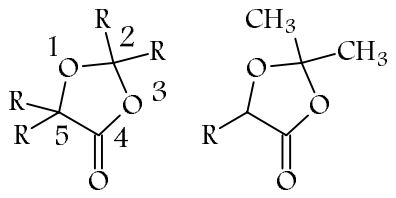
Chapter Three

2,2-Dimethyl-[1,3]dioxolan-4-ones

3.1 General introduction

For the work on mandelamides described in Chapter Two, a range of mandelamides substituted on the phenyl ring were required. As has been discussed in Chapter Two, there is no quick and easy method of preparing these amides from the acids. In this Chapter we will demonstrate that 2,2-dimethyl-[1,3]dioxolan-4-ones can react under mild conditions with ammonia to give the amide, and with other amines to give substituted amides. This aminolysis has not been widely used, which is surprising since a large variety of reactions on these dioxolanones has been reported and some of these will be discussed in this Chapter.



3.1 3.2

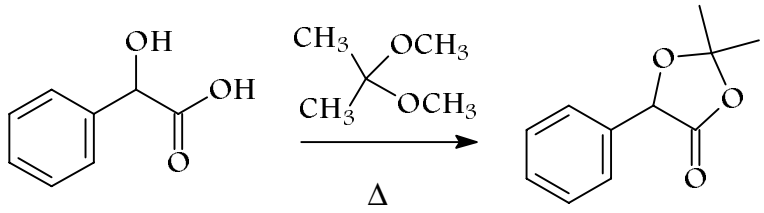
Scheme 1: The general structure and numbering system of dioxolanones.

3.2.1 Introduction to [1,3]dioxolan-4-ones

An α-hydroxy acid will condense with aldehydes and ketones under acidic conditions with azeotropic removal of water formed during the reaction. The resulting heterocycle, a dioxolanone, has the general structure 3.1 in Scheme 1. This condensation works best with acetone and the product is a 2,2-dimethyl-[1,3]dioxolan-4-one (3.2 in Scheme 1). Because it is the result of the reaction of a hydroxy acid with acetone, it is often called an "acetonide" of the acid. The five membered ring is subject to substitution at positions 2,4 and 5.

3.2.2 Methods of preparation of 2,2-dimethyl-dioxolanones

Although the condensation works best with acetone, the reported yield is not always very high and one is left with the acidic catalyst which has to be removed.[1] The use of a solid acidic heterogeneous catalyst like a Dowex resin or a zeolite seems not to have been described for this reaction.



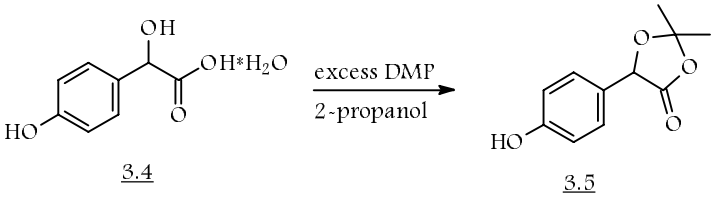
3.3

Scheme 2: Reaction of mandelic acid with dimethoxy propane to give 3.3.

To increase yields, the acetone has to be made more reactive. Acetone, as its dimethyl acetal which is commercially available, is highly activated towards nucleophilic attack. As is shown in Scheme 2, reaction of the free hydroxy acid in a transacetalization with acetone-dimethylacetal (2,2-dimethoxypropane, DMP) gives the acetonide 3.3 without need of an acidic catalyst, thereby making the work-up easier.[2] Only the evaporation of the excess DMP and solvents is necessary.[a] The reaction is quick and we find that it is nearly quantitative.

The reaction with DMP can be performed in all kinds of solvents although benzene and cyclohexane are preferred because they form an azeotropic mixture with the methanol that is produced during the reaction, which can then be distilled off. Some hydroxy acids are not soluble in these apolar solvents. In that case, more polar solvents like acetonitrile and even 2-propanol can be employed. We used 2-propanol in the reaction of DMP with 4-hydroxy-mandelic acid monohydrate 3.4, which does not dissolve in aprotic solvents, to give acetonide 3.5, which is illustrated in Scheme 3.

[a]Although DMP is not exactly cheap at Fl 55/500 ml, it is considerably cheaper than some of the hydroxy acids it has to react with.

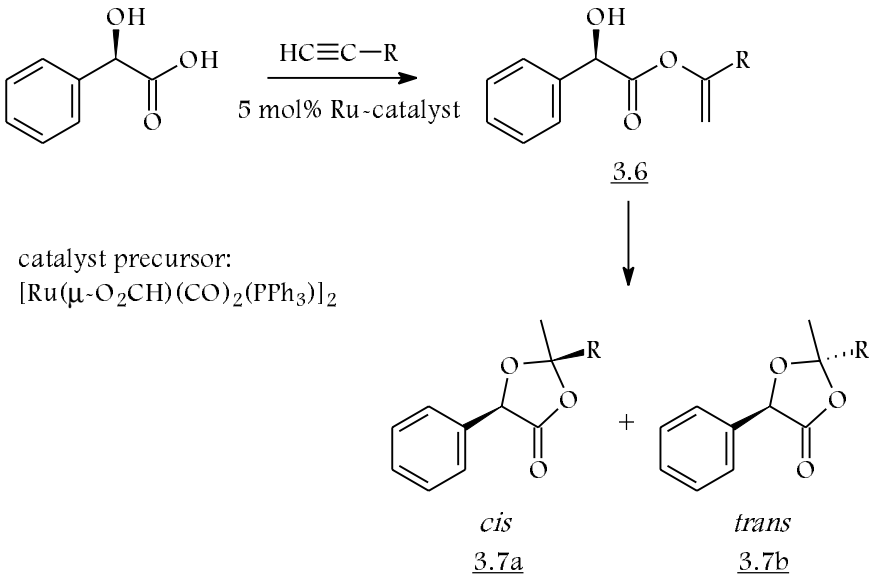


Scheme 3: Acetalization in an alcohol.

Later we found that the reaction without a solvent works also very well. Simply heating the reaction mixture to a temperature that lies above the boiling point of methanol is enough to effect reaction. This procedure may be more expensive but it has the advantage of being much quicker than the one using solvents.

Another interesting way of synthesizing these dioxolanones is shown in Scheme 4. Several organometallic reagents that catalyze acetal formation have been reported but they are all based on the reaction of an aldehyde or ketone with an alcohol or diol.[3] The method in Scheme 4 is based on a quite different mechanism.

A ruthenium catalyzed reaction between a hydroxy acid, for example, mandelic acid, and a terminal alkyne provides 3.6 which undergoes ring closure on heating to give 3.7a and 3.7b.[4] The reported yields are not quantitative but the diastereoselectivity is

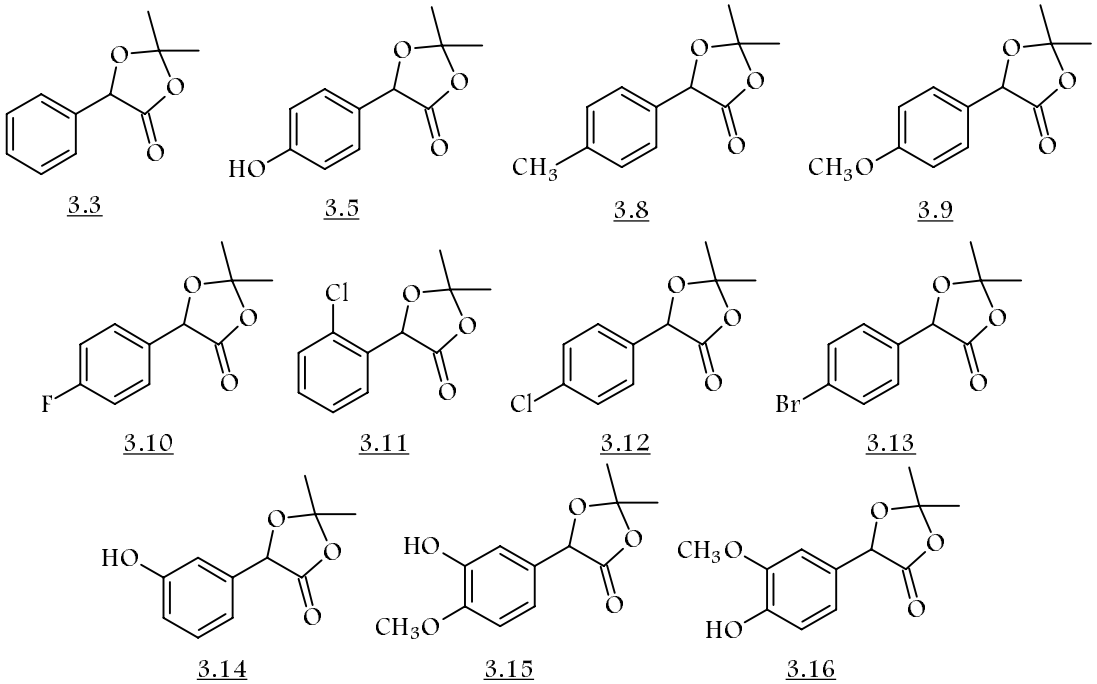


Scheme 4: Ruthenium catalyzed formation of dioxolanones.

in most cases very good. The ratio between the two possible products, *cis* and *trans* 3.7, ranges from 75/25 to 95/5. This is about the same selectivity that has been reported by Seebach[5] in the condensation of mandelic acid with pivalaldehyde (section 3.3). Also no racemization was observed when the intermediate enol ester 3.6 was hydrolyzed back to the starting hydroxy acid. When propyne is used, dioxolanone 3.3 is obtained in 70% yield.

3.2.3 Reactivity of hydroxy acids with DMP: substituent effect and properties of the dioxolanones

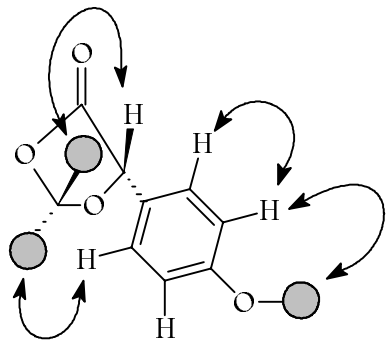
Because they were required as precursors to the amides described in Chapter Two, the acetonides of a range of substituted mandelic acids were prepared and these are shown in Scheme 5. These compounds are, with a few exceptions, all low melting solids. This can be a drawback in some syntheses, though for most purposes the acetonide need not be isolated and purified. If the solid acetonide is wanted, it has to be washed carefully with 1N $NaHCO_3$ solution to remove any unreacted acid and DMP. Either hydrolysis to the acid occurs readily or the washing procedure is not perfect, for some acid is always left, making the elemental analysis a little off the mark. The analyses for carbon are systematically too low.



Scheme 5: The structures of the synthesized dioxolanones.

As a rule of thumb, we found that halogen substituents on the phenyl ring have a retarding effect, both on the rate of formation of the dioxolanone and on the rate of the ring opening with ammonia. This finding caused us to look further into the properties of these compounds.

As is clear from the proton NMR, and also from the ^{13}C NMR, the signals for the diastereotopic methyl groups at the 2-position of the five membered ring are separated. NOESY NMR spectroscopy clearly shows the different environments of the methyl groups also. The higher field methyl group has an interaction with the α-proton of the hydroxy acid (position 4), whereas the downfield methyl group has an interaction with the phenyl ring. This is illustrated in Scheme 6. The chemical shift difference between the methyl groups is not equal for every compound. This is due to the different anisotropy effect of the phenyl ring, depending on the substituent, which gives different amounts of shielding. The chemical shift differences Δδ are given in Table 1.

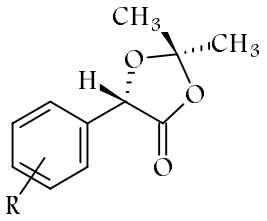


3.15

Scheme 6: Arrows show the NOE interactions in compound 3.15. Grey balls represent methyl groups.

The clear difference in reactivity between the non-halogenated and the halogenated compounds could be the result of ring strain. FT-IR spectra were recorded to investigate the strain in the five membered ring of the dioxolanones. The IR absorbance of a carbonyl group in a cyclic compound shifts to higher wave numbers in rings that show more strain.[6] From the IR values (Table 1) it can be concluded that there is no substantial difference in ring strain throughout the range of compounds and that this is not the origin of the different reactivities.

Table 1: ^{1}H NMR shift differences[#] between the methyl groups and FT-IR absorptions of the carbonyl groups[§].



Compound	R=	Relative reactivity	Δδ (ppm)	ν (cm^{-1})
3.11	2-Cl	-	0.074	1786
315	4-OMe, 3-OH	+	0.064	1778
3.9	4-OMe	++	0.057	1792
3.5	4-OH	+	0.057	1771
3.16	3-OMe, 4-OH	+	0.055	1765
3.8	4-Me	+	0.053	1784
3.14	3-OH	n.s.*	0.053[ǂ]	1788
3.3	H	+/-	0.049	1796
3.10	4-F	-	0.048	1778
3.12	4-Cl	-	0.041	1778
3.13	4-Br	-	0.038	1782

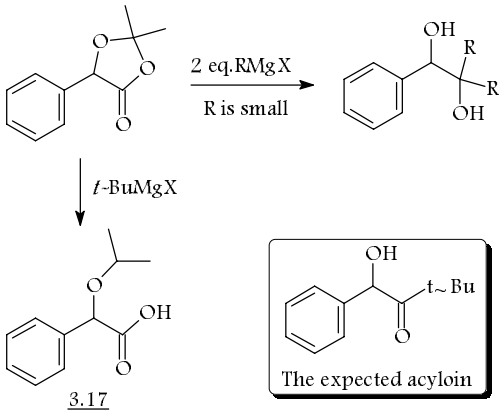
[#]300 MHz NMR ($CDCl_3$); [§]KBr pellet; *n.s. not obtained as a solid;
[ǂ]10% CD_3OD added for solubility.

If the ring strain is equal in each compound, then the difference in reaction rate must arise from the substituents on the phenyl ring. The halogen atoms have some kind of *negative* influence on the reactivity of the carbonyl group in the five membered ring. The other way around, it can be stated that oxygen containing substituents have a *positive* effect on the reactivity. How this effect should be explained is not clear at present but it definitely is there. Further proof for the existence of a rate enhancing effect of donating substituents comes from the fact that if the phenyl ring is moved one carbon atom farther away from the dioxolanone ring, the reactivity drops to zero (3.40, shown in section 3.5). Apparently the rate enhancing influence can be exerted no longer.

3.3 The reactivity of the dioxolanones reviewed. Ring opening, alkylation, addition, reduction and other reactions

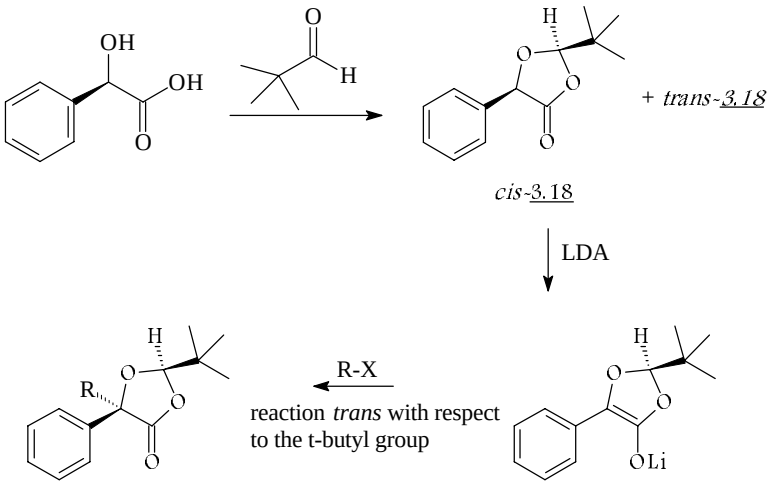
The acetonide ring can be opened with alcohols under acidic circumstances. If the ester is the desired product, protection and alcoholysis can be combined into one reaction step. Thus, synthesis of mandelic acid esters can be accomplished in a one-pot procedure by heating the acid, DMP and an alcohol to give, after work-up, the ester.[7] The acetonide can also react with amines[8], though a slightly different method has to be followed when amines are to be used because an amine can react with DMP to form the imine. Therefore, prior to reaction with an amine, the excess DMP must be removed, which is easily done by evaporation. When the amine is added, either liquid or gaseous, usually the reaction is completed very quickly. The aminolysis of the dioxolanones will be treated more extensively in section 3.4.

Besides ring opening, these dioxolanones can undergo several other reactions. The molecule is in fact an ester and it is not surprising that it can react with Grignard reagents to give glycols as is shown in Scheme 7.[9] Reaction of the acetonide with a Grignard reagent with high steric requirements, which was expected to give a Grignard mono-addition product, led to a quite different result. Not the expected acyloin was formed but α-isopropoxy mandelic acid 3.17, the result of a reductive cleavage of the ring.[9] This reductive cleavage was only found for *t*-butylmagnesium halides; the formation of isobutylene is observed, consistent with reduction via β-hydride loss from the *t*-butyl group.



Scheme 7: The action of Grignard reagents on dioxolanones.

The α-proton of the dioxolanone is acidic enough to be easily removed with LDA. The resulting enolate can be quenched with an electrophile to give the alkylated acetonide. Opening this acetonide in a standard way gives the alkylated hydroxy acid.[10] Seebach has described this alkylation method for the production of *enantiomerically pure* α-alkylated hydroxy acids (Scheme 8).[5] A diastereoselective condensation of enantiomerically pure mandelic acid with pivalaldehyde gives dioxolanone 3.18. The ratio between *cis* and *trans* varies from 3:1 to 9:1. The thermodynamically controlled *cis*-product is obtained pure after crystallization.



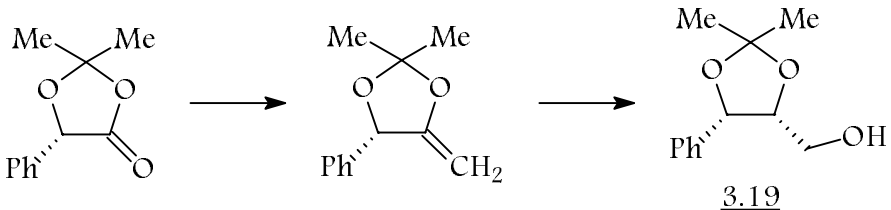
Scheme 8: Seebach's self-reproduction of chirality.

Deprotonation of this compound gives the lithium enolate which reacts diastereo-selectively with an electrophile to give the alkylated acetonide back. Here, the tertiary butyl group directs the synthesis towards the trans diastereomer. The arrangement around the stereogenic center stays intact; only the proton is substituted for the electrophile. Seebach refers to this as "Self-Regeneration of Stereocenters" (SRS)[11].

In another type of reaction, the carbonyl group of the dioxolanone can be transformed with the Tebbe methylenation reagent[a] to a double bond that can be diastereoselectively hydroborated followed by oxidation to give product 3.19 (shown in Scheme 9). The resulting product is a 1-phenylglycerol.[12] Starting from the same

[a]μ-Chloro-μ-methylene-[bis(cyclopentadienyl)titanium]dimethylaluminium.

dioxolanone, via a different route, it is also possible to prepare 2-phenyl-glycerols, as has been shown by Hof *et al.*[8]



3.19

Scheme 9: Methylenation followed by hydroboration gives 3.19.

3.4 Reaction of dioxolanones with ammonia or other amines; a neglected route to (substituted) hydroxy amides

As was expected, all of the dioxolanones shown in Scheme 5 can be opened with ammonia to give the primary amides shown in Scheme 10. Here we present the fast method that was needed in section 2.6.1:

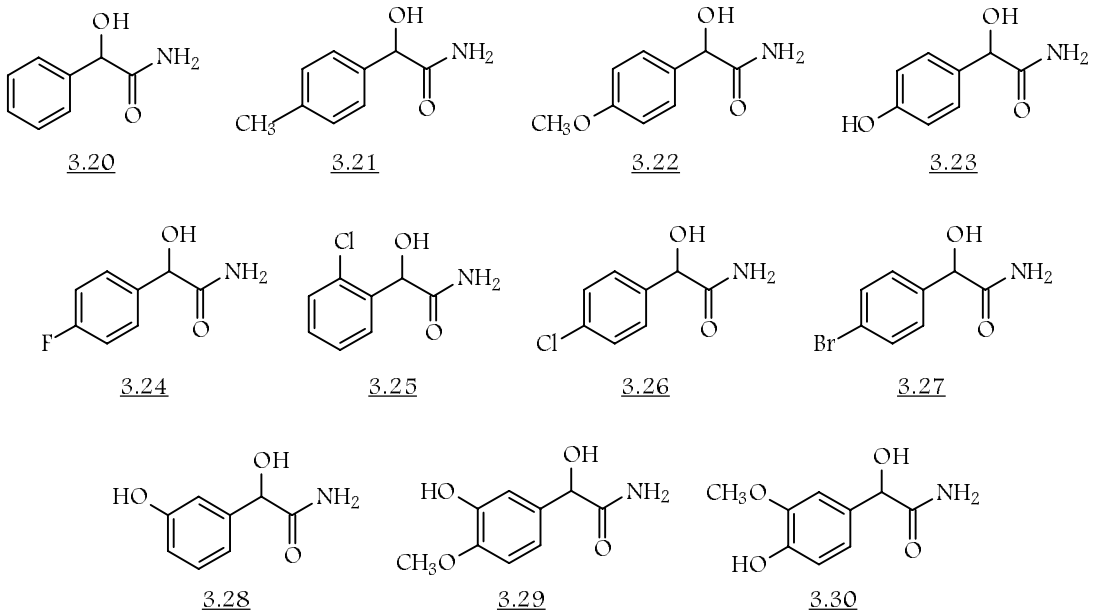
> *Mandelic acid is treated with neat DMP at 75 °C for 15 minutes. Evaporation of excess DMP and passage of a stream of ammonia gas through a methanolic acetonide solution*[a] *for 5 minutes gives, after evaporation of the volatiles, the amide in 95% overall yield within half an hour!*

Although sometimes an aqueous solution of ammonia is used, the best results have been obtained with methanol as a solvent and gaseous ammonia. Especially with the hydroxy-phenyl substituted acetonides, use of an aqueous ammonia solution is not favorable. The reaction mixture becomes dark and the product is very sticky. Perhaps the ammonia acts as a base and deprotonates the hydroxy functionality or the product is partially oxidized to an α-ketoamide. The hydroxy-methoxy substituted mandelic acids are air sensitive and should be stored under argon. This is the reason a satisfactory melting point is not found for compound 3.30, which probably is not stable

[a] Though these are basic conditions under which attack of an alcoholate is possible, we never found alcoholysis of the acetonide to give the ester. Any ester formed can also react with ammonia to the amide but this is a much slower process and some accumulation of ester is possible.

and is oxidized on standing (to an ortho quinone?). Aminolysis of compound 3.14 resulted in complex reaction mixtures and the synthesis of 3.28 was not pursued further.

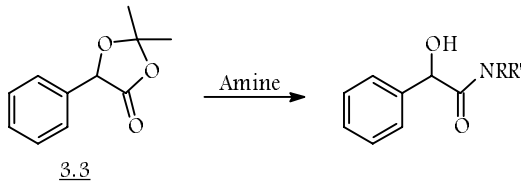
The concentration of saturated NH_3 in methanol is high enough to facilitate reaction. Other solvents like toluene or benzene are less able to dissolve the NH_3 but have the advantage that the produced amide is sparingly soluble and crystallizes readily. Reaction in these apolar solvents takes more ammonia and is slower but the product is obtained simply by filtration. The use of methanol is mildly preferred.



Scheme 10: An overview of the prepared amides.

Since the ring opening of the acetonides worked very well with ammonia, we wanted to expand the synthetic use of this method to other amines. Only very little is known about this reaction. Khalaj and co-workers described the reaction of dioxolanone 3.3 with four amines: propyl amine, 2-amino-pyridine, aniline and 4-nitro-aniline. The reaction requires harsh conditions like reflux in xylene or heating in a sealed tube for prolonged periods.[13] The reaction with more hindered secondary amines is therefore expected to be even more sluggish. To investigate this, we allowed acetonide 3.3 to react with several amines as is shown in Table 2.

Table 2: Reaction of 3.3 with several amines.



3.3

Amine	Product	Yield[#]
CH_3NH_2	3.31	82%
$(CH_3)_2NH$	3.32	65%
$(CH_3CH_2)_2NH$	3.33	53%[$]
$H_2NNH_2{*}H_2O$	3.34	74%
n-butylamine	3.35	60%
iso-propylamine	3.36	62%
benzylamine	3.37	70%
cyclohexylamine	3.38	55%

[#]These are yields after crystallization. In most cases no residual acetonide was detected.

[$]Obtained as a clear oil after chromatography.

It is known that aniline and aniline derivatives are not the most reactive amines and they need forcing reaction conditions but the harsh conditions that Khalaj describes for propylamine certainly are not necessary. The eight amines that we have tested all reacted with the acetonide at room temperature. Only the reaction with diethylamine, to give 3.33, was very slow at this low temperature. After standing for ten days there still was about 10 percent of acetonide left. The product is reported to be an oil[1], which is surprising since all other amides of mandelic acid that we prepared are crystalline solids. However, all efforts to crystallize the compound were in vain.

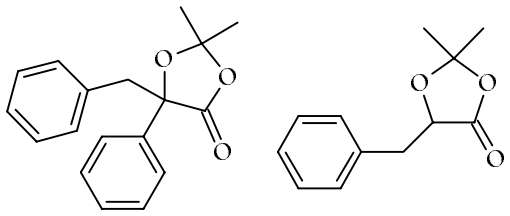
Most amides in Table 2 are known compounds that have been prepared from the ester or acid chloride. Since the method described in this section has some definite advantages over the classical preparations, it is surprising that it has not been explored further.

We feel that this route can be applied to almost every primary amine and some (less hindered) secondary amines.

3.5 Reaction of some other dioxolanones with ammonia

We prepared also a few α-alkylated acetonides via the LDA-procedure described in section 3.3, of which one example (3.39, Scheme 11) is shown. In trying to open the five membered ring with gaseous ammonia, we ran into problems. The extra alkyl group causes severe steric hindrance and reduces the reactivity drastically. Also the acetonide of 3-phenyl lactic acid, 3.40, resisted reaction with ammonia. In this case, it should be more of an electronic effect than a steric effect since the phenyl group is one carbon atom farther away from the carbonyl group.

In a different experiment hexamethyldisilazane (HMDS) was used in place of NH_3. Although it is much less nucleophilic, the advantage of HMDS is that it is a liquid having a relatively high boiling point of 125 °C and the reactions can be performed at elevated temperatures. However, although HMDS served our purpose well in Chapter 4, here we had no success.



3.39 3.40

Scheme 11: Dioxolanones that resist reaction with ammonia or HMDS.

3.6 Summary

In this Chapter we have demonstrated that the synthesis of hydroxy amides, starting from the corresponding hydroxy acids, can be performed in a straightforward procedure via the 2,2-dimethyl-[1,3]dioxolan-4-ones. The great advantage of this method is that it is quick and proceeds via stable intermediates. As we have shown, this greatly neglected protection-activation scheme can be applied to the synthesis of other

amides as well, which was not surprising. In most cases the yield of amide was very good, giving only some problems for secondary amines.

Substitution of the α-hydrogen atom for an alkyl group makes the dioxolanone much less reactive. To produce the amide, the five membered ring has to be opened with an alcohol under acidic conditions to give the ester which can then be aminated. However, these amides can also be prepared from the esters, thereby making the acetonide pathway unnecessary.

3.7 Experimental section (see Chapter Two for general remarks)

2,2-Dimethyl-5-phenyl-[1,3]-dioxolan-4-one 3.3

Mandelic acid (100 gr, 0.66 mol) is heated in a mixture of cyclohexane and 75 gr DMP (1.1 eq.) under Dean Stark reflux. After 2.5 hours, the mixture is evaporated, giving a clear oil that slowly solidifies. Yield: 115 gr (0.60 mol, 91%). Mp. 40 °C (Uncorr., Lit.[11] 48 °C). ^{1}H NMR ($CDCl_3$) δ 1.68 (s, 3H, CH_3); 1.73 (s, 3H, CH_3); 5.40 (s, 1H, CH); 7.38-7.45 (m, 5H, CH). ^{13}C NMR ($CDCl_3$) δ 26.1 (CH_3); 27.1 (CH_3); 76.3 (CH); 110.8 (C_q); 126.3 (CH); 128.6 (CH); 128.8 (CH); 133.6 (C_q); 177.4 (CO). FT-IR (KBr) 1796 cm^{-1} (CO).

5-(4-Methoxy-phenyl)-2,2-dimethyl-[1,3]dioxolan-4-one 3.4

4-Methoxy-mandelic acid (2.00 gr, 11.0 mmol) is stirred with 15 ml 2,2-dimethoxy-propane at 60 °C for two hours. The solvents are evaporated off and the residue is taken up in diethyl ether. After washing with 1N $NaHCO_3$ and drying on sodium sulphate, the ether is evaporated. The resulting white solid is recrystallized from 2-propanol. Yield 1.83 gr (10.7 mmol, 97%). Mp. 35 °C (Uncorr.), Bp 185 °C (decomp.). ^{1}H NMR ($CDCl_3$) δ 1.65 (s, 3H, CH_3); 1.71 (s, 3H, CH_3); 3.80 (s, 3H, CH_3); 5.34 (s, 1H, CH); 6.92 (d, J= 8.6 Hz, 2H, CH); 7.35 (d, J= 8.6 Hz, 2H, CH). ^{13}C NMR ($CDCl_3$) δ 25.9 (CH_3); 27.1 (CH_3); 55.2 (CH_3); 75.7 (CH); 110.5 (C_q); 114.1 (CH); 126.3 (C_q); 128.0 (CH); 160.0 (C_q); 171.6 (CO). FT-IR (KBr) 1792 cm^{-1} (CO). Anal. Calcd. for $C_{12}H_{14}O_4$: H, 6.35; C, 64.85; O, 28.80. Found: H, 6.24; C, 64.43.

5-(4-Hydroxy-phenyl)-2,2-dimethyl-[1,3]dioxolan-4-one 3.5

4-Hydroxy-mandelic acid monohydrate (5.00 gr, 26.9 mmol) is taken up in 25 ml cyclohexane with 10 ml 2-propanol. DMP (5.60 gr, 54 mmol) is added and the mixture is refluxed under Dean Stark conditions. The reaction is stopped when a constant reflux temperature is reached and the solvents are evaporated, giving a brown oil. This is taken up in ether and washed with 1N $NaHCO_3$. After drying and evaporation, a white solid is obtained. Yield: 5.25 gr (25.2 mmol, 94%). Mp. 88-89 °C (Uncorr.). ^{1}H NMR (DMSO-d6) δ 1.59 (s, 3H, CH_3); 1.64 (s, 3H, CH_3); 5.55 (s, 1H, CH); 6.78 (d, J= 8.3 Hz, 2H, CH); 7.18 (d, J= 8.5 Hz, 2H, CH); 9.65 (brs, 1H, OH). ^{13}C NMR (DMSO-d6) δ 25.4 (CH_3); 26.7 (CH_3); 75.5 (CH); 110.2 (C_q); 115.5 (CH); 125.3 (C_q); 129.0 (CH); 158.2 (C_q); 172.3 (CO). FT-IR (KBr) 1771 cm^{-1} (CO). Anal. Calcd. for $C_{11}H_{12}O_4$: H, 5.81; C, 63.45; O, 30.74. Found: H, 5.54; C, 60.70.

2,2-Dimethyl-5-p-tolyl-[1,3]dioxolan-4-one 3.8

4-Methyl-mandelic acid (2.00 gr, 12.0 mmol) is stirred with 15 ml 2,2-dimethoxy-propane at 60 °C for two hours. The solvents are evaporated off and the residue is taken up in diethyl ether. After washing with 1N $NaHCO_3$ and drying on sodium sulphate, the ether is evaporated. The resulting white solid is recrystallized from 2-propanol, giving a low-melting solid. Yield: 2.17 gr (11.2 mmol, 88 %). Mp. 50-51 °C (Uncorr.), Bp. 156 °C (decomp.). ^{1}H NMR ($CDCl_3$) δ 1.83 (s, 3H, CH_3); 1.89 (s, 3H, CH_3); 2.53 (s, 3H, CH_3); 5.53 (s, 1H, CH); 7.38 (d, J= 8.1 Hz, 2H, CH); 7.51 (d, J= 8.1 Hz, 2H, CH). ^{13}C NMR ($CDCl_3$) δ 21.1 (CH_3); 26.0 (CH_3); 27.2 (CH_3); 75.8 (CH); 110.7 (C_q); 126.4 (CH); 129.3 (CH); 131.4 (C_q); 138.8 (C_q); 171.6 (CO). FT-IR (KBr) 1784 cm^{-1} (CO). Anal. Calcd. for $C_{12}H_{14}O_3$: H, 6.84; C, 69.89; O, 23.27. Found: H, 6.79; C, 69.76.

5-(4-Fluor-phenyl)-2,2-dimethyl-[1,3]dioxolan-4-one 3.10

This compound was kindly provided by Dr. R.P. Hof. ^{1}H NMR ($CDCl_3$) δ 1.67 (s, 3H, CH_3); 1.72 (s, 3H, CH_3); 5.37 (s, 1H, CH); 7.09 (m, 2H, CH); 7.44 (m, 2H, CH). ^{13}C NMR ($CDCl_3$) δ 25.9 (CH_3); 27.1 (CH_3); 75.1 (CH); 110.9 (C_q); 115.5 (CH); 115.8

(CH); 128.1 (CH); 128.2 (CH); 130.1 (C_q); 161.3 (C_q); 171.1 (CO). ^{19}F NMR ($CDCl_3$) δ -114.5. ^{19}F NMR (DMSO-d6) δ -110.0. FT-IR (KBr) 1778 cm^{-1} (CO).

5-(2-Chloro-phenyl)-2,2-dimethyl-[1,3]dioxolan-4-one 3.11

2-Chloromandelic acid (5.00 gr, 26.8 mmol) is reacted with 4.18 gr 2,2-dimethoxy propane (1.5 eq, 40.2 mmol) in 50 ml cyclohexane. The mixture is heated until the reflux temperature is that of pure DMP. Then the rest of the solvent is distilled off. The resulting cream coloured oil solidifies. Mp 68-70 °C (Uncorr.). Yield: 6.00 gr (26.6 mmol, 99%). ^{1}H NMR (DMSO-d6) δ 1.66 (s, 3H, CH_3); 1.70 (s, 3H, CH_3); 5.95 (s, 1H, CH); 7.41-7.55 (m, 4H, CH). ^{13}C NMR (DMSO-d6) δ 25.2 (CH_3); 26.1 (CH_3); 74.0 (CH); 111.0 (C_q); 127.7 (CH); 130.2 (CH); 131.2 (CH); 131.3 (CH); 131.8 (C_q); 133.2 (C_q); 170.6 (CO). FT-IR (KBr) 1786 cm^{-1} (CO). Anal. Calcd. for $C_{11}H_{11}ClO_3$: H, 4.89; C, 58.29; O, 21.18; Cl, 15.64. Found: H, 4.88; C, 58.07.

5-(4-Chloro-phenyl)-2,2-dimethyl-[1,3]dioxolan-4-one 3.12

4-Chloromandelic acid (5.00 gr, 26.8 mmol) is reacted with 5.60 gr 2,2-dimethoxy-propane (2.0 eq, 53.8 mmol) in 15 ml cyclohexane under Dean Stark conditions. The mixture is heated until the reflux temperature is that of pure DMP (about two hours). Then the rest of the solvent is distilled off, giving a white solid. Yield: 5.26 gr (23.2 mmol, 87%). Mp. 67-69 °C (Uncorr.). ^{1}H NMR (DMSO-d6) δ 1.64 (s, 3H, CH_3); 1.68 (s, 3H, CH_3); 5.76 (s, 1H, CH); 7.45 (d, J= 8.8 Hz, 2H, CH); 7.50 (d, J= 8.8 Hz, 2H, CH). ^{13}C NMR (DMSO-d6) δ 25.4 (CH_3); 26.6 (CH_3); 74.7 (CH); 110.8 (C_q); 128.7 (CH); 133.6 (C_q); 133.8 (C_q); 171.2 (CO). FT-IR (KBr) 1778 cm^{-1} (CO). Anal. Calcd. for $C_{11}H_{11}ClO_3$: H, 4.89; C, 58.29; O, 21.18; Cl, 15.64. Found: H, 4.69; C, 57.78; O, 21.35.

5-(4-Bromo-phenyl)-2,2-dimethyl-[1,3]dioxolan-4-one 3.13

4-Bromomandelic acid (5.00 gr, 21.6 mmol) is stirred in 10 ml DMP in 50 ml cyclohexane. This is refluxed until a constant boiling point is reached. The residual solvents are evaporated giving a white solid. Yield: 5.65 gr (20.8 mmol, 97%). Mp. 58-60 °C (Uncorr., Lit.[9] 65 °C). ^{1}H NMR (DMSO-d6) δ 1.63 (s, 3H, CH_3); 1.67 (s, 3H,

CH_3); 5.74 (s, 1H, CH); 7.37 (d, J= 8.3 Hz, 2H, CH); 7.63 (d, J= 8.3 Hz, 2H, CH). ^{13}C NMR (DMSO-d6) δ 25.6 (CH_3); 26.8 (CH_3); 74.9 (CH); 111.1 (C_q); 122.5 (C_q); 129.4 (CH); 132.0 (CH); 134.5 (C_q); 171.5 (CO). FT-IR (KBr) 1782 cm^{-1} (CO).

5-(3-Hydroxy-phenyl)-2,2-dimethyl-[1,3]dioxolan-4-one 3.14

3-Hydroxy-mandelic acid (500 mg, 2.98 mmol) is heated with 5 ml DMP at 70 °C for two hours. Solvents are evaporated, giving a brownish oil that fails to crystallize from methanol/ether. Yield 610 mg (2.93 mmol, 98%). ^{1}H NMR (DMSO-d6) δ 1.62 (s, 3H, CH_3); 1.66 (s, 3H, CH_3); 5.61 (s, 1H, CH); 6.75-6.85 (m, 3H, CH); 7.21 (t, J= 8.0 Hz, 1H, CH); 9.61 (brs, 1H, OH). ^{13}C NMR (DMSO-d6) δ 25.5 (CH_3); 26.7 (CH_3); 75.3 (CH); 110.6 (C_q); 113.8 (CH); 115.9 (CH); 117.6 (CH); 129.8 (CH); 136.3 (C_q); 157.7 (C_q); 171.7 (CO). FT-IR (KBr) 1788 cm^{-1} (CO).

5-(3-Hydroxy-4-methoxy-phenyl)-2,2-dimethyl-[1,3]dioxolan-4-one 3.15

The acid (500 mg, 2.53 mmol) is heated in 5 ml DMP at 70 °C for 30 minutes. Evaporation of the solvents and crystallization from methanol/ether gives the product as a white solid. Yield: 552 mg (2.32 mmol, 92%). Mp. 66-68 °C (Uncorr.). ^{1}H NMR ($CDCl_3$) δ 1.65 (s, 3H, CH_3); 1.71 (s, 3H, CH_3); 3.88 (s, 3H, OCH_3); 5.29 (s, 1H, CH); 5.70 (s, 1H, OH); 6.90-6.95 (m, 3H, CH). ^{13}C NMR ($CDCl_3$) δ 25.8 (CH_3); 27.0 (CH_3); 55.8 (CH); 75.6 (CH_3); 110.4 (CH); 110.6 (C_q); 112.7 (CH); 118.6 (CH); 127.4 (C_q); 145.7 (C_q); 146.3 (C_q); 171.4 (CO). FT-IR (KBr) 1778 cm^{-1} (CO). Anal. Calcd. for $C_{12}H_{14}O_5$: H, 5.92; C, 60.50; O, 33.58. Found: H, 5.79; C, 58.96.

5-(4-Hydroxy-3-methoxy-phenyl)-2,2-dimethyl-[1,3]dioxolan-4-one 3.16

The acid (500 mg, 2.53 mmol) is heated in 5 ml DMP to 70 °C. After 30 minutes, the solvents are evaporated off. The resulting oil is taken up in methanol (1 ml) and ether (3 ml) is added. Upon cooling, the product crystallizes. Further manipulation of the motherliquor gives another portion of product. Yield: 590 mg (2.48 mmol, 98%). Mp. 109-110 °C (Uncorr.). ^{1}H NMR ($CDCl_3$) δ 1.65 (s, 3H, CH_3); 1.70 (s, 3H, CH_3); 3.88 (s, 3H, OCH_3); 5.32 (s, 1H, CH); 5.76 (s, 1H, OH); 6.90-6.95 (m, 3H, CH). ^{13}C NMR

($CDCl_3$) δ 25.8 (CH_3); 27.0 (CH_3); 55.7 (CH); 75.8 (C_q); 108.9 (CH); 110.6 (C_q); 114.4 (CH); 119.8 (CH); 126.0 (C_q); 146.2 (C_q); 146.6 (C_q); 171.7 (CO). FT-IR (KBr) 1765 cm^{-1} (CO). Anal. Calcd. for $C_{12}H_{14}O_5$: H, 5.92; C, 60.50; O, 33.58. Found: H, 5.87; C, 59.46.

2-Hydroxy-2-phenyl-acetamide 3.20

The acetonide (70.0 gr, 0.36 mol) was dissolved in 100 ml methanol. Ammonia gas is bubbled through this solution for 30 minutes. The mixture becomes slightly orange. Evaporation of the solvents gives a yellow solid which is recrystallized from 2-propanol. Yield: 48.6 gr (0.32 mol, 88%). Mp. 127-128 °C (Uncorr., Lit.[14] 132 °C). ^1H NMR (DMSO-d6) δ 4.85 (d, J= 4.5 Hz, 1H, CH); 6.01 (d, J= 4.8 Hz, 1H, OH); 7.15 (brs, 1H, NH); 7.22-7.43 (m, 6H, CH/NH). ^{13}C NMR (DMSO-d6) δ 73.5 (CH); 126.5 (CH); 127.3 (CH); 127.9 (CH); 141.4 (C_q); 174.6 (CO).

2-Hydroxy-2-p-tolyl-acetamide 3.21

The acetonide of 4-methyl mandelic acid (1.00 gr, 4.85 mmol) is dissolved in 15 ml benzene. $NH_3(g)$ is bubbled through the solution for a few minutes. This mixture is left standing overnight. The product crystallizes from this solution as clear white needles. The product is filtered off. Concentrating the motherliquor gives another crop of pure product. Yield: 680 mg (4.12 mmol, 85%). Mp. 124-125 °C (Uncorr., Lit.[15] 129-130 °C). ^1H NMR (DMSO-d6) δ 2.27 (s, 3H, CH_3); 4.78 (d, J= 4.4 Hz, 1H, CH); 5.91 (d, J= 4.4 Hz, 1H, OH); 7.12 (d, J= 8.1 Hz, 2H, CH); 7.15 (brs, 1H, NH); 7.29 (d, J= 8.1 Hz, 2H, CH), 7.34 (brs, 1H, NH). ^{13}C NMR (DMSO-d6) δ 20.7 (CH3); 73.2 (CH); 126.4 (CH); 128.4 (CH); 136.4 (C_q); 138.5 (C_q); 174.7 (CO).

2-Hydroxy-2-(4-methoxy-phenyl)-acetamide 3.22

The acetonide (1.05 gr, 4.73 mmol) is dissolved in 15 ml methanol. Ammonia gas is bubbled through the solution for two minutes. This is left standing overnight during which the product crystallizes as a very fine powder. This is recrystallized from 2-propanol to give clear needles. Yield: 790 mg (4.36 mmol, 92%). Mp. 159-160 °C (Uncorr., Lit.[16] 162-163 °C). ^1H NMR (DMSO-d6) δ 3.72 (s, 3H, CH_3); 4.76 (d, J= 4.4

Hz, 1H, CH); 5.86 (d, J= 4.5 Hz, 1H, OH); 6.88 (d, J= 8.4 Hz, 2H, CH); 7.13 (brs, 1H, NH); 7.32 (d, J= 8.4 Hz, 2H, CH); 7.33 (brs, 1H, NH).
^{13}C NMR (DMSO-d6) δ 55.1 (CH_3); 73.0 (CH); 113.3 (CH); 127.7 (CH); 133.5 (C_q); 158.6 (C_q); 174.8 (CO).

2-Hydroxy-2-(4-hydroxy-phenyl)-acetamide 3.23

The acetonide (510 mg, 2.45 mmol) is dissolved in 2 ml methanol. Ammonia gas is led through the solution for 5 minutes. Evaporation of the solvent gives a yellow solid. Recrystallization from methanol/ether gives the product. Yield: 310 mg (1.67 mmol, 68%). Mp. 120-121 °C (Uncorr., Lit.[17] 145 °C for the hydrate). ^{1}H NMR (DMSO-d6) δ 4.69 (d, J= 4.4 Hz, 1H, CH); 5.77 (d, J= 4.4 Hz, 1H, OH); 6.68 (d, J= 8.4 Hz, 2H, CH); 7. 10 (brs, 1H, NH); 7.17 (d, J= 8.4 Hz, 2H, CH); 7.28 (brs, 1H, NH); 9.31 (brs, 1H, OH). ^{13}C NMR (DMSO-d6) δ 73.2 (CH); 114.6 (CH); 127. 8 (CH); 131.8 (C_q); 156.7 (C_q); 175.0 (CO).

2-Hydroxy-2-(4-fluor-phenyl)-acetamide 3.24

The acetonide (1.05 gr, 5.0 mmol) is dissolved in 15 ml methanol. Ammonia gas is bubbled through the solution for two minutes. Standing overnight gives the product which crystallizes from 2-propanol as clear plates. Yield: 830 mg (4.9 mmol, 98%). Mp. 148-150 °C (Uncorr.). ^{1}H NMR (DMSO-d6) δ 4.83 (d, J= 4.2 Hz, 1H, CH); 6.07 (d, J= 4.6 Hz, 1H, OH); 7.14 (t, J= 9.2 Hz, 2H, CH); 7.19 (brs, 1H, NH); 7.43 (dd, J= 9.2 Hz, J= 9.2 Hz, 3H, CH/NH). ^{13}C NMR (DMSO-d6) δ 72.7 (CH); 114.4 (CH); 114.7 (CH); 128.3 (CH); 128.4 (CH); 137.6 (C_q); 163.1 (C_q); 174.4 (CO). ^{19}F NMR (DMSO-d6) δ -112.5. Anal. Calcd. for $C_8H_8NO_2F$: H, 4.77; C, 56.80; N, 8.28; O, 18.92; F, 11.23. Found: H, 4.81; C, 56.65; N, 8.23.

2-Hydroxy-2-(2-chloro-phenyl)-acetamide 3.25

The acetonide (3.37 gr, 14.9 mmol) is dissolved in 50 ml CH_2Cl_2. Ammonia gas is bubbled through the solution for 15 minutes. A white precipitate is formed. After standing for one hour the solvents are evaporated giving a white solid that is recrys-

tallized from benzene as white needles. Yield: 2.67 gr (14.4 mmol, 97%). Mp. 82-83 °C (Uncorr., Lit.[18] 87 °C). ^{1}H NMR (DMSO-d6) δ 5.22 (d, J= 4.8 Hz, 1H, CH); 6.23 (d, J= 5.1 Hz, 1H, OH); 7.31-7.47 (m, 6H, CH/NH).

^{13}C NMR (DMSO-d6) δ 70.3 (CH); 127.1 (CH); 128.9 (CH); 129.0 (CH); 129.1 (CH); 132.7 (C_q); 139.1 (C_q); 173.6 (CO).

2-Hydroxy-2-(4-chloro-phenyl)-acetamide 3.26

The acetonide (2.50 gr, 11.0 mmol) is dissolved in 15 ml MeOH. Concentrated ammonia is added and the mixture is left standing overnight. Evaporation of the solvents gives the pure white product. Yield: 1.97 gr (10.6 mmol, 96%). Mp. 112-113 °C (Uncorr., Lit.[19] 126 °C). ^{1}H NMR (DMSO-d6) δ 4.81 (s, 1H, CH); 7.20 (brs, 1H, NH); 7.31-7.45 (m, 5H, CH/NH). ^{13}C NMR (DMSO-d6) δ 72.6 (CH); 127.8 (CH); 128.2 (CH); 131.8 (C_q); 140.3 (C_q); 174.1 (CO).

2-Hydroxy-2-(4-bromo-phenyl)-acetamide 3.27

The acetonide (2.50 gr, 9.23 mmol) is dissolved in 20 ml toluene. NH_3 (g) is bubbled through and a white precipitate forms. This is recrystallized from acetonitrile. Yield: 1.80 gr (7.84 mmol, 85%). Mp. 135-136 °C (Uncorr., Lit.[20] 141 °C). ^{1}H NMR (DMSO-d6) δ 4.83 (s, 1H, CH); 6.13 (brs, 1H, OH); 7.21 (brs, 1H, NH); 7.37 (d, J= 8.4 Hz, 2H, CH); 7.41 (brs, 1H, NH); 7.51 (d, J= 8.4 Hz, 2H, CH). ^{13}C NMR (DMSO-d6) δ 78.1 (CH); 125.8 (C_q); 134.0 (CH); 136.2 (CH); 146.2 (C_q); 179.5 (CO).

2-Hydroxy-2-(4-methoxy-3-hydroxy-phenyl)-acetamide 3.29

The acetonide (440 mg, 1.85 mmol) is taken up in 5 ml dry methanol. Ammonia gas is led through the solution, which is left standing for 60 minutes. Evaporation gives a solid that is recrystallized from acetonitrile. Yield: 290 mg (1.47 mmol, 80%). Mp. 141-143 °C (Uncorr.). ^{1}H NMR (DMSO-d6) δ 3.68 (s, 3H, CH_3); 4.64 (d, J= 3.1 Hz, 1H, CH); 5.76 (d, J= 4.0 Hz, 1H, OH); 6.73-6.82 (m, 3H, CH); 7.09 (brs, 1H, NH); 7.25 (brs, 1H, NH); 8.87 (brs, 1H, OH). ^{13}C NMR (DMSO-d6) δ 55.7 (CH_3); 73.1 (CH); 111.7 (CH); 114.0 (CH); 117.5 (CH); 134.1 (C_q); 146.1 (C_q); 147.0 (C_q); 174.8 (CO).

Anal. Calcd. for $C_9H_{11}NO_4$: H, 5.62; C, 54.82; N, 7.10; O, 32.45. Found: H, 5.68; C, 54.70; N, 6.87.

2-Hydroxy-2-(3-methoxy-4-hydroxy-phenyl)-acetamide 3.30

Obtained in the same procedure as for 3.29 from 520 mg (2.18 mmol) acetonide. Yield: 400 mg (2.03 mmol, 93%). Mp. 95-99 °C (Uncorr.). ^{1}H NMR (DMSO-d6) δ 3.71 (s, 3H, CH_3); 4.69 (s, 1H, CH); 5.80 (brs, 1H, OH); 6.67 (d, J= 8.0 Hz, 1H, CH); 6.76 (d, J= 7.8 Hz, 1H, CH); 6.94 (s, 1H, CH); 7.09 (brs, 1H, NH); 7.31 (brs, 1H, NH); 8.85 (brs, 1H, OH). ^{13}C NMR (DMSO-d6) δ 55.6 (CH_3); 73.4 (CH); 110.8 (CH); 114.9 (CH); 119.1 (CH); 132.4 (C_q); 145.9 (C_q); 147.1 (C_q); 175.0 (CO). Anal. Calcd. for $C_9H_{11}NO_4$: H, 5.62; C, 54.82; N, 7.10; O, 32.45. Found: H, 5.69; C, 53.71; N, 6.89.

N-Methyl-2-hydroxy-2-phenyl-acetamide 3.31

The acetonide (500 mg, 2.60 mmol) is kept overnight in 5 ml of a 33% solution of methylamine in ethanol at room temperature. After evaporation of the solvents, a brown solid is obtained that is recrystallized from benzene. Yield: 350 mg (2.10 mmol, 82%). Mp. 85-87 °C (Uncorr., Lit.[21] 96-99 °C). ^{1}H NMR (DMSO-d6) δ 2.57 (s, 1.5 H, CH_3); 2.59 (s, 1.5H, CH_3); 4.87 (d, J= 3.7 Hz, 1H, CH); 6.12 (d, J= 4.4 Hz, 1H, OH); 7.24-7.40 (m, 5H, CH); 7.95 (brs, 1H, NH). ^{13}C NMR (DSMO d6) δ 25.4 (CH_3); 73.6 (CH); 126.5 (CH); 127.3 (CH); 127.9 (CH); 141.4 (C_q); 172.6 (CO).

N,N-Dimethyl-2-hydroxy-2-phenyl-acetamide 3.32

The acetonide (500 mg, 2.60 mmol) is dissolved in 5 ml 40% dimethylamine in water. This mixture is left standing overnight and the product crystallizes as fine needles. Yield: 300 mg (1.70 mmol, 65%). Mp. 153-154 °C (Uncorr., Lit.[22] 158 °C). ^{1}H NMR (DMSO-d6) δ 2.82 (s, 3H, CH_3); 2.83 (s, 3H, CH_3); 5.36 (d, J= 6.2 Hz, 1H, CH); 5.43 (d, J= 6.3 Hz, 1H, OH); 7.27-7.34 (m, 5H, CH). ^{13}C NMR (DMSO-d6) δ 35.4 (CH_3); 36.1 (CH_3); 70.8 (CH); 126.9 (CH); 127.6 (CH); 128.4 (CH); 140.3 (C_q); 171.8 (CO).

N,N-Diethyl-2-hydroxy-2-phenyl-acetamide 3.33

The acetonide (500 mg, 2.60 mmol) is taken up in 1.0 ml diethylamine and left standing for ten days. The mixture turns red. Evaporation of the excess amine gives a red oil that is taken up in diethyl ether and washed with 1N HCl. The ether is dried and evaporated. After column chromatography (SiO_2, ϕ 2 cm, l= 5 cm, ether), a clear oil is obtained. Yield: 285 mg (1.38 mmol, 53%). ^{1}H NMR ($CDCl_3$) δ 0.78 (t, J= 9.5 Hz, 3H, CH_3); 1.06 (t, J= 9.5 Hz, 3H, CH_3); 3.05-3.42 (m, 4H, CH_2); 4.57 (brs, 1H, OH); 5.08 (s, 1H, CH); 7.22-7.39 (m, 5H, CH). ^{13}C NMR ($CDCl_3$) δ 12.4 (CH_3); 12.8 (CH_3); 40.6 (CH_2); 40.8 (CH_2); 71.3 (CH); 127.3 (CH); 128.3 (CH); 128.8 (CH); 139.6 (C_q); 171.2 (CO).

2-Hydroxy-2-phenyl-acetic acid hydrazide 3.34

The acetonide (500 mg, 2.6 mmol) is kept overnight in 2.5 ml hydrazine hydrate. After evaporation of the solvent and recrystallization from water the product is obtained as clear plates. Yield: 320 mg (1.90 mmol, 74%). Mp. 128-130 °C (Uncorr., Lit.[23] 91-92 °C). ^{1}H NMR (DMSO-d6) δ 4.20 (brs, 2H, NH_2); 4.91 (d, J= 5.1 Hz, 1H, CH); 5.95 (d, J= 5.1 Hz, 1H, OH); 7.20-7.43 (m, 5H, CH); 9.14 (brs, 1H, NH). ^{13}C NMR (DMSO-d6) δ 72.8 (CH); 126.5 (CH); 127.4 (CH); 127.9 (CH); 141.4 (C_q); 171.2 (CO).

N-Butyl-2-hydroxy-2-phenyl-acetamide 3.35

The acetonide (500 mg, 2.60 mmol) is dissolved in 5 ml diethylether. Butylamine is added (1.0 gr) and this is left standing overnight. Evaporation of the solvent gives a clear oil. This is taken up in ether and washed with 1N HCl. Drying and evaporation gives a white solid which is recrystallized from 2-propanol. Yield: 320 mg (1.55 mmol, 60%). Mp. 47-49 °C (Uncorr.). ^{1}H NMR (DMSO-d6) δ 0.83 (t, J=7.3 Hz, 3H, CH_3); 1.22 (m, 2H, CH_2); 1.35 (m, 2H, CH_2); 3.04 (q, J= 6.5 Hz, 2H, CH_2); 4.85 (d, J= 3.6 Hz, 1H, CH); 6.08 (d, J= 4.5 Hz, 1H, OH); 7.24-7.40 (m, 5H, CH); 7.95 (brs, 1H, NH). ^{13}C NMR (DMSO-d6) δ 13.6 (CH_3); 19.4 (CH_2); 31.2 (CH_2); 37.8 (CH_2); 73.5 (CH); 126.5 (CH); 127.2 (CH); 127.8 (CH); 141.5 (C_q); 171. 8 (CO).

2-Hydroxy-N-isopropyl-2-phenyl-acetamide 3.36

The acetonide (500 mg, 2.60 mmol) is mixed with 1 ml isopropylamine. After overnight standing at room temperature, the mixture is taken up in ether and washed with 1N HCl. Drying and evaporation gives the product which is recrystallized from diethyl-ether. Yield: 310 mg (1.61 mmol, 62%). Mp. 78-79 °C (Uncorr., Lit.[24] 80-81 °C). ^{1}H NMR (DMSO-d6) δ 1.03 (t, J= 6.3 Hz, 6H, CH_3); 3.81 (h, J= 7.5 Hz, 1H, CH); 4.83 (d, J= 3.6 Hz, 1H, CH); 6.05 (d, J= 3.6 Hz, 1H, OH); 7.22-7.38 (m, 5H, CH); 7.69 (d, J= 7.8 Hz, 1H, NH). ^{13}C NMR (DMSO-d6) δ 22.2 (CH_3); 40.1 (CH); 73.4 (CH); 126.5 (CH); 127.4 (CH); 127.8 (CH); 141.5 (C_q); 171.0 (CO).

N-Benzyl-2-hydroxy-2-phenyl-acetamide 3.37

The acetonide (5.00 gr, 26.0 mmol) is dissolved in 50 ml toluene. Two equivalents of benzylamine are added (5.60 gr). This is stirred for 30 minutes at 60 °C. On cooling, the product crystallizes. Filtrating and rinsing with diethyl ether gives the product. Yield: 4.30 gr (17.84 mmol, 70%). Mp. 94-95 °C (Uncorr., Lit.[25] 99-100 °C). ^{1}H NMR (DMSO-d6) δ 4.27 (d, J= 6.4 Hz, 2H, CH_2); 4.97 (d, J= 4.2 Hz, 1H, CH); 6.22 (d, J= 4.6 Hz, 1H, OH); 7.46-7.15 (m, 10H, CH); 8.55 (t, 1H, NH). ^{13}C NMR (DMSO-d6) δ 41.9 (CH_2); 73.8 (CH); 126.9 (CH); 127.0 (CH); 127.4 (CH); 127.7 (CH); 128.2 (CH); 128.5 (CH); 139.9 (C_q); 141.6 (C_q); 172.6 (CO).

N-Cyclohexyl-2-hydroxy-2-phenyl-acetamide 3.38

The acetonide (500 mg, 2.6 mmol) is dissolved in 2.5 ml methanol with 1.00 gr cyclohexylamine (10.1 mmol). This gives a red solution that is left standing overnight at room temperature. Some product crystallizes. The mixture is taken up in ether and washed three times with 1N HCl. Drying and evaporation gives 400 mg of an off-white solid which is recrystallized from diethyl ether. Yield: 335 mg (1.42 mmol, 55%). Mp. 89-90 °C (Uncorr.). ^{1}H NMR (DMSO-d6) δ 1.00-1.30 (m, 5H, CH_2); 1.45-1.70 (m, 5H, CH_2); 3.35 (s, 1H, CH); 4.83 (d, J= 5.1 Hz, 1H, CH); 6.04 (d, J= 5.1 Hz, 1H, OH); 7.21-7.37 (m, 5H, CH); 7.67 (d, J= 8.4 Hz, 1H, NH). ^{13}C NMR (DMSO-d6) δ 24.6 (CH_2); 25.1 (CH_2); 32.2 (CH_2); 47.2 (CH); 73.3 (CH); 126. 5 (CH); 127.3 (CH); 127.9 (CH); 141.9 (C_q); 171.0 (CO). Anal. Calcd. for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00; O, 13.72. Found: C, 71.76; H, 8.19; N, 5.98.

5-Benzyl-5-phenyl-2,2-dimethyl-[1,3]dioxolan-4-one 3.39

Prepared from acetonide 3.3 and benzylbromide as a clear oil, following standard procedures.[26] Yield: 65% (after Kugelrohr distillation). ^{1}H NMR ($CDCl_3$) δ 1.11 (s, 3H, CH_3); 1.39 (s, 3H, CH_3); 3.22 (AB, ^{1}J= 65 Hz, ^{2}J= 14 Hz, 2H, CH_2); 7.19-7.40 (m, 8H, CH); 7.75 (d, J= 7.8 Hz, 2H, CH). ^{13}C NMR ($CDCl_3$) δ 26.9 (CH_3); 27.8 (CH_3); 47.7 (CH_2); 84.2 (C_q); 110.7 (C_q); 124.7 (CH); 127.0 (CH); 127.9 (CH); 128.3 (CH); 128.5 (CH); 130.9 (CH); 134.9 (C_q); 140.0 (C_q); 165.0 (CO).

5-Benzyl-2,2-dimethyl-[1,3]-dioxolan-4-one 3.40

3-Phenyl-lactic acid (1.00 gr, 6.02 mmol) is heated to 75 °C in 5 ml DMP for two hours. After this period, the solvents are evaporated and the acetonide is taken up in ether and washed with 1N $NaHCO_3$. Drying and evaporation gives the product which is recrystallized from ethanol as clear needles. Yield: 1.05 gr (5.10 mmol, 85%). Mp. 61-62 °C (Uncorr., Lit.[27] 63-64°C). ^{1}H NMR ($CDCl_3$) δ 1.36 (s, 3H, CH_3); 1.50 (s, 3H, CH_3); 3.13 (AB, ^{1}J= 44.1 Hz, ^{2}J= 4.2 Hz, 2H, CH_2); 4.66 (dd, 1H, CH); 7.25-7.32 (m, 5H, CH). ^{13}C NMR ($CDCl_3$) δ 26.0 (CH_3); 26.8 (CH_3); 37.5 (CH_2); 74.9 (CH); 110.8 (C_q); 126.9 (CH); 127.2 (CH); 128.3 (CH); 135.6 (C_q); 172.4 (CO).

3.8 References

1. B.L. Karlsson, C.L. Haakanson, M. Nilsson, A. Hedlund, Chem. Abstr., *124*, P260606: SE 502722, Dec 18th, **1995**
2. H. Takahashi, N. Murakami, Chem. Abstr., *120*, P216993: JP92-101255, Apr 21st, **1992**
3. F. Gorla, L.M. Venanzi, Helv. Chim. Acta, *73*, 690, **1990**
4. M. Neveux, B. Seiller, F. Hagedorn, C. Bruneau, P.H. Dixneuf, J. Organomet. Chem., *451*, 133, **1993**
5. D. Seebach, R. Naef, G. Calderari, Tetrahedron, *40*, 1313, **1984**; G. Frater, U. Müller, W. Günther, Tetrahedron Lett., *22*, 4421, **1981**
6. M. Hesse, H. Meier, B. Zeeh, Spektroskopische Methoden in der Organischen Chemie, 2nd Ed., Georg Thieme Verlag, Stuttgart, **1984**
7. R. Chenevert, M. Letourneau, Can. J. Chem., *68*, 314, **1990**
8. H. Oeda, Bull. Chem. Soc. Jpn., *11*, 385, **1936**
9. R.C. Fuson, A.I. Rachlin, J. Am. Chem. Soc., *64*, 1567, **1942**
10. R.P. Hof, R.M. Kellogg, J. Org. Chem., *61*, 3423, **1996**; H. Moorlag, J.G. de Vries,

B. Kaptein, H.E. Schoemaker, J. Kamphuis, R.M. Kellogg, Recl. Trav. Chim. Pays-Bas, *111*, 129, **1992**

11. For a review on SRS: D. Seebach, A.R. Sting, M. Hoffmann, Angew. Chem., Int. Ed. Engl., *35*, 2708, **1996**
12. E. Untersteller, Y.C. Xin, P. Sinay, Tetrahedron Lett., *35*, 2537, **1994**
13. A. Khalaj, E. Nahid, Synthesis, 1153, **1985**
14. C.F. Audrieth, M. Sveda, Org. Synth., *20*, 62, **1940**
15. S. Akihama, M. Okude, Chem. Abstr., *69*, 10167, **1968**
16. A. McKenzie, D.J.C. Pirie, Ber., *69B*, 861, **1936**
17. G. Taborsky, P.S. Cammarata, J.S. Fruton, J. Biol. Chem., *226*, 103, **1957**
18. S.S. Jenkins, J. Am. Chem. Soc., *53*, 2341, **1931**
19. F. Straus, Ann., *393*, 235-337, p.p. 320, **1912**
20. Y. Naka, K. Shigezane, Chem. Abstr., *70*, 11290, **1969**
21. G.G. Lyle, J. Org. Chem., *25*, 1779, **1960**
22. K. Freudenberg, J. Todd, R. Seidler, Ann., *501*, 199, **1933**
23. A. Gvozdjakova, J. Schnittova, Chem. Abstr., *66*, 37602
24. R.F. Rekker, W. Th. Nauta, Recl. Trav. Chim. Pays-Bas, *70*, 241, **1951**
25. K. Matsumoto, S. Hashimoto, T. Uchida, T. Okamoto, S. Otani, Chem. Ber., *122*, 1357, **1989**
26. H. Moorlag, Chiral α-substituted α-hydroxy acids, PhD. thesis, University of Groningen, **1991**
27. H. Oeda, Bull. Chem. Soc. Jpn., *10*, 187, **1935**